ANIMAL MODEL FOR HUMAN DISEASE

Spina Bifida, Sacral Dysgenesis and Myelocele

Animal Model: Manx Cats

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Manx are a clownish breed of cat said to originate on the Isle of Man. Easily distinguishable by a variety of biologic and morphologic characteristics, they are most noted for their absence of a tail. However, a peculiar autosomal dominant trait[1] provides the genetic basis not only for taillessness and the related traits so prized by cat fanciers, but also for a number of associated anomalies. Few people realize that the unique appearance of the Manx actually constitutes the observable, relatively normal end of a spectrum of genetically controlled breed characteristics which include many serious deficiencies and potentially lethal abnormalities.

Biologic Features

Both the "normal" and "abnormal" characteristics express themselves in a wide variety of phenotypes.[2,3] This intraspecies variation is most readily evident with respect to tail length. Common Manx characteristics are disproportionately long hind legs, short back, large round head, round-shaped rump and a distinctive rabbity humpy gait. Manx cats of show quality must be completely tailless in addition to possessing these other traits, but Manx litters generally yield some kittens with normal tails, some with short tails ("stumpies"), and others with a mere remnant of cartilaginous material ("high-riser"), as well as the tailless "rumpies" who completely lack coccygeal vertebrae. The hollow at the base of the backbone in "rumpies" indicates total coccygeal agenesis.

Despite their unusual physique, many Manx cats grow to be successful show animals or delightful pets without signs of any other remarkable disorders. The Manx breeder, however, soon discovers that a considerable percentage of the kittens suffer from severe congenital abnormalities primarily related to spinal lesions. These abnormalities range from fecal and urinary incontinence to a variety of severe spinal lesions—everything from agenesis of the sacrum to agenesis of the coccygeal

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vertebrae, absence of cauda equina, etc.[4] Such kittens generally must be euthanatized.

James *et al*[4] has reported that the monoplegic Manx cat demonstrates a medial rotation of the metatarsal homologous to the inversion and cavovarus associated with abnormalities of the human foot; this abnormality causes the distinctive hopping gait in affected Manx cats. The severely affected cat can travel quickly in a straight line but tends to fall over when changing direction. Whether the peculiar incoordination of the hind legs is due to the abnormal pelvic posture or to longer than normal length of the hind legs is not known.

Most frequently animals with the coccygeal agenesis but normal sacrum are free from any clinical disability; however, they can show a variety of abnormalities without severe hind-limb paralysis. Three cats who exhibited sacral dysgenesis were found by James *et al*[4] to be either monoplegic or incontinent in the urine or feces, or both. In one case where severe defect of the sacrum was associated with incomplete dorsal laminae (spina bifida), the lower cord of cauda equina was united with the meninges and covered only a subcutaneous fat and skin resembling a myelocele in man.[4] The abnormalities of the sacrum cauda equina explain the incontinence of urine and feces.

These reports have stimulated the development of a colony of Manx cats here at the Center for Laboratory Animal Resources. At the present time, the study has included 6 males and 2 females. Three of the animals have died during this period. Necropsy of these animals was performed. The predominant lesion in the first cat was obstruction of the pelvic urethra. The second cat had a history of urinary and fecal incontinence and was lacking its coccygeal vertebrae. Changes in the terminal urinary and intestinal tracts supposedly resulted from functional or anatomical deficiencies in innervation. The predominant lesion of the third cat was coccygeal agenesis; the spinal cord appeared somewhat shortened, the cauda equinae being found in the midsacral region. The cauda equinae was not fused with the meninges; hence, there was no strong resemblance to myelocele or spina bifida in man. Sections of spinal cord from the sacral, lumbar, thoracic and cervical areas were histiologically normal, and lacked the dorsal cord lesions associated with human dysraphism.

Of the remaining animals, 2 males exhibit no clinical abnormalities; 1 female has the very distinct hopping gait and previously had 3 litters of kittens—cesarean section was necessary with all but 1 litter. Only 2 kittens from the litters lived past 3 months of age. The need for cesarean section was a result of uterine inertia, which may represent lack of normal nerve innervation. One kittten developed severe clinical signs of abdominal distention and urinary and fecal incontinence.

Figure 1 demonstrates one of the more obvious clinical signs, the oc-

currence of abnormal distention of abdominal cavity and accumulation of fecal material and distinct intestine dilatation. Dysgenesis or sacrococcygeal agenesis is shown in Figure 2.

Comparison with Spina Bifida

Paraplegia and hind limb monoplegia in Manx cats are similar to the clinical syndrome in some cases of human spina bifida occulta. Spina bifida, a cleft in the spine, is a congenital abnormality attributed to the

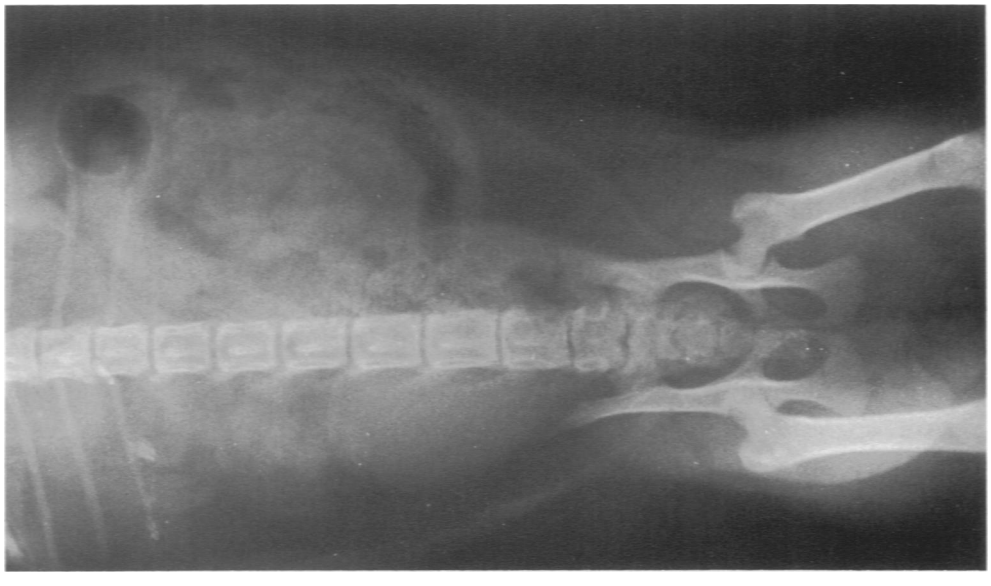

Fig 1—X-ray of a 4-month-old male Manx cat. Note the abnormal distention of the abdominal cavity due to the accumulation of fecal material and intestinal dilation.

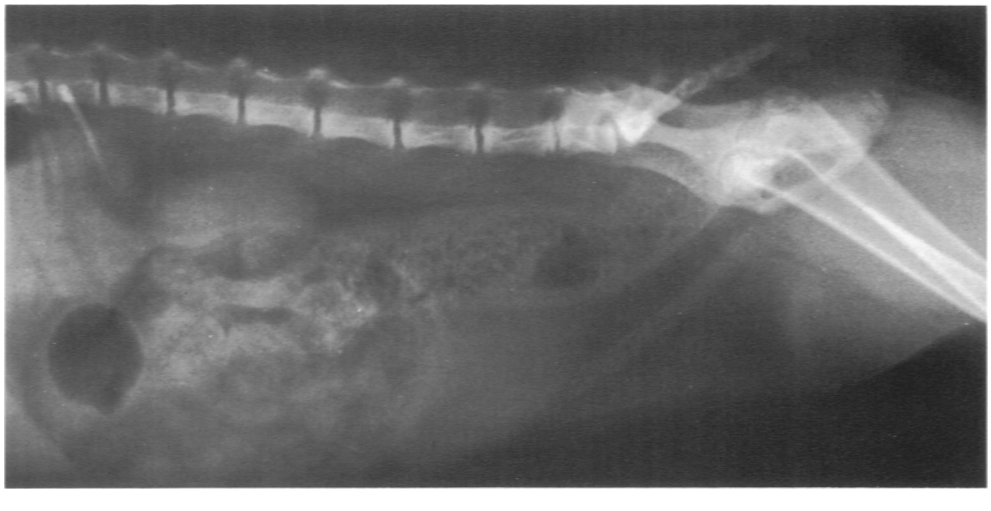

Fig 2—X-ray of a 6-month-old Manx cat. Note the agenesis of the coccygeal bones.

incomplete fusion of the laminae to form the vertebral arches. In man and in cats there may be a steady deterioration after birth; the organism becomes paraplegic or partially disabled and many remain stationary.[5]

Kerruish was the first to describe some of the pathologic characteristics of the Manx cat and compared them with spina bifida in man.[5] The Manx cat would seem to be a particularly valuable animal model not only for the study of spina bifida but also for understanding the variable expression of simple autosomal alleles. Further, there is the possibility of associating these various abnormalities with behavorial characteristics. These possibilities indicate the Manx to be a highly desirable biomedical model which merits further investigation.

Spina bifida and sacrococcygeal agenesis have been described in other cat breeds,[6, 7] as well as in Swiss mice, calves, dogs and sheep.[8, 9] Experimentally induced spina bifida using trypan blue has also been described.[10] The occurrence of spontaneous abnormalities with a predominant high frequency certainly underlines the logical use of the Manx cats for biomedical models.

Availability

Manx cats are uncommon but certainly not rare; breeders can be found in most areas of the United States. The spontaneous lesions, described here, are increased by breeding rumpy phenotypes to rumpy phenotypes.

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